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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/083,825	02/27/2002	Roger K. Khouri	STK-066C2 (7557/36)	8501

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EXAMINER	
NAFF, DAVID M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/083,825	KHOURI ET AL.	
	Examiner	Art Unit	
	David M. Naff	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/11 & 3/10/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-106* is/are pending in the application.

4a) Of the above claim(s) *34-48,54 and 61-69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-53, 55-60 & 70-106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

In a response of 2/11/04 to a restriction requirement of 1/9/04, an amendment amended claims 49-53, 55-60 and 70, added new claims 71-106 which are dependent on claims in Group II, and elected Group II claims 49-53, 55-60 and 70 with traverse.

The traverse is on the ground that claims 45-48 included in Group I should be rejoined with the claims of Group II since no more work is required to examine the invention of claims 45-48. However, claims 45-48 require a different invention of repairing a skeletal joint defect using a matrix including bone as set forth in the restriction requirement, and examining this invention will require a substantial amount of additional work that will constitute a serious burden on the examiner. The restriction requirement is adhered to and made final.

Claims 34-48, 54 and 61-69 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response of 2/11/04.

Since new claims 71-106 are dependent on Group II claims, these claims are included with the claims of Group II.

Claims examined on the merits are 49-53, 55-60 and 70-106.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

Applicant is advised that should claim 70 be found allowable, claim 85 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 70 and 85 are identical.

Claim Objections

Claims 49, 50, 55 and 56 are objected to because of the following informalities: the claims are not properly amended by not underlining all additions. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51-53, 57-59, 74-76, 80-82, 86-88, 92-94 and 97-102 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention.

The recitations "fibrovascular tissue", "anterior cruciate ligament" and "functional attachment site of tendon or ligament to bone" in the above dependent claims are not found in the specification. Adequate support is not found in the specification for further limiting of the matrix as required by the dependent claims.

Claim Rejections - 35 USC § 112

Claims 49-53, 55-60 and 70-106 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the plural distinct tissues of the matrix being a body part containing plural distinct tissues that have been devitalized by extracting cellular non-structural components from the tissues of the body part to produce an acellular matrix having interstices that can be infiltrated by cells, does not reasonably provide enablement for another form of plural distinct tissues. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification discloses only a form of plural distinct tissues as set forth above. No other form of plural distinct tissues has been described that can form the matrix. It would be unpredictable and speculation as to other forms of plural distinct tissues that will function to form the matrix.

Claim Rejections - 35 USC § 112

Claims 49-53, 55-60 and 70-106 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The meaning and scope of "plural distinct tissues" recited in the claims is uncertain. It is uncertain as to the way in which the plural tissues are combined, and whether the tissues occur in the body or are tissues different from body tissues. If different, it is uncertain as to how the tissues differ.

Claim 55 is unclear by in the last line requiring the structure to permit regeneration of articular cartilage in a skeletal joint, and not requiring in the claim preamble the articular cartilage defect repaired to be in a skeletal joint. It is uncertain as to the purpose of stating that regeneration of articular cartilage in a skeletal joint can occur in the last line if the defect repaired as required in the preamble is not in a skeletal joint.

In dependent claims where recited, it is uncertain as to tissue that provides "fibrovascular tissue" and "anterior cruciate ligament", and the form of matrix that provides a "functional attachment site of tendon or ligament to bone" since the specification fails to recite and define tissue and an attachment site as required by these claims.

Dependent claims 60, 77, 83, 89, 95, 103 and 106 are unclear as to how the device contains the materials required by the claims in relation to the osteogenic protein and matrix of the device required

by independent claims. Are the materials of the claims separate from the protein and matrix, or are they combined with the protein and matrix in some way. The contiguous relationship of these materials with the osteogenic protein and matrix should be set forth to be clear as to the device claimed when the materials are present. In line 2 of these claims, the meaning of "butyric glycolic acid" is uncertain. Is this a copolymer of butyric and glycolic acid or is something else intended. Should butyric acid be recited as a separate acid from glycolic acid?

In claims 71, 72, 78, 84, 90, 96, 104 and 105 "devitalized" is uncertain as to meaning and scope. Being devitalized is relative and subjective, and it would be uncertain as to tissue that is and is not devitalized within the scope of the claim.

Claim Rejections - 35 USC § 103

Claims 49-53, 55-60 and 70-106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oppermann et al (5,258,494) (AT on form 1449) in view of Goldstein (5,899,936) and Bishopric et al (5,855,620) and Livesey et al (5,336,616).

Claim 49 and claims dependent thereon are drawn to a device for implantation in a mammal which serves as a template for forming in vivo articular cartilage tissue. The device comprises exogenous osteogenic protein disposed on a surface of a matrix comprising plural distinct tissues including articular cartilage tissue defining a structure that allows for infiltrating cells. Claim 50 and claims dependent thereon claim the same type of device for in vivo

replacement of non-mineralized tissue wherein the plural distinct tissues include at least one non-mineralized tissue. Claims 55 and 56 and claims dependent thereon are drawn to methods of using the devices for repairing in a mammal an articular cartilage defect and a non-mineralized tissue defect in a skeletal joint.

Oppermann et al disclose an osteogenic device comprising a matrix containing an osteogenic protein that can be used for inducing cartilage formation (col 3, lines 12-13 and 40-43) in an avascular locus (col 4, lines 49-52 and col 10, lines 62-64). The matrix can be demineralized bone or a matrix material containing collagen (col 9, lines 56-65). The osteogenic protein can have 6 or 7 cysteine residues, or be Vg1, DPP or OP1 (paragraph bridging cols 5 and 6, and col 7, lines 45-65).

Goldstein discloses (col 2, lines 41-67) producing tissue for implanting in mammals. The tissue is decellularized to produce an acellular tissue matrix (col 4, line 25 to col 7, line 55). The decellularized tissue matrix is treated with a cellular adhesion factor to enhance cell attachment (col 7, line 58 to col 9, line 24) and repopulated with cells (col 9, line 25 to col 10, line 3). Examples of tissues that can be used are heart valves , fascia lata, dura mater, pericardium, meniscus, skin, ligament, tendon, and other connective tissue structures (col 3, lines 14-20). The initial tissue or organ may be of non-human origin (col 3, lines 64-67). Immunologically active molecules are removed so the tissue matrix does

not produce an adverse immune response by a recipient upon implantation (col 2, lines 45-50).

Bishopric et al disclose producing a transplant tissue by decellularizing body tissue to form an extracellular matrix having intact collagen and elastin components, and which can be recellularized in vitro or in vivo (col 3, lines 46-50) and provide for ingrowth of host cells following implantation (col 3, lines 40-43). The tissue may be a heart valve (col 5, line 15).

Livesey et al disclose (col 1, lines 17-39) decellularizing tissue to produce an extracellular protein matrix made up of collagen and other proteins to provide a structural template that can be repopulated with new cells in vitro or in vivo (col 6, lines 63-64). Antigenic tissue components are removed so the tissue does not elicit an immune response by a host in which the tissue is implanted (col 4, lines 24-25 and 50-55).

When the matrix of Oppermann et al is material containing collagen, it would have been obvious to use as the matrix the decellularized tissue matrix disclosed by Goldstein, Bishopric et al and Livesey et al since this matrix is an extracellular protein matrix made of collagen and would have been expected to provide the function of a matrix desired by Oppermann et al. Additionally, the decellularized tissue matrix does not elicit an immune response and would have been expected to be advantageous for this result. Having the osteogenic protein on the surface of the matrix would have been obvious to make the protein readily available to function. The matrix

containing an osteogenic protein of Oppermann et al can be used for cartilage repair at an avascular locus, and it would have been obvious repair articular cartilage since this is an avascular cartilage. When repairing articular cartilage and using decellularized tissue as the matrix, it would have been obvious to decellularize tissue containing articular cartilage since Goldstein, Bishopric et al and Livesey et al decellularize tissue from a location where new tissue is to be generated. Decellularized tissue produced as disclosed by Goldstein, Bishopric et al and Livesey et al inherently contains plural distinct tissues. Cartilage tissue is a non-mineralized tissue, and generating cartilage tissue as suggested by Oppermann et al produces non-mineralized tissue. The tissues and osteogenic proteins of dependent claims would have been matters of obvious choice in view of the disclosures of the references. Bishopric et al suggest vascular tissue (col 5, lines 14-15), and the specific vascular tissue of claim 51 would have been obvious. Goldstein suggests ligament or tendon tissue (col 3, line 19), and the specific ligament or tendon tissue of claims 52 and 53 would have been obvious. Decellularized ligament or tendon tissue will inherently have an attachment site as in claim 53. The decellularized tissue inherently contains collagen as in claim 60. Oppermann et al suggest hydroxyapatite and a copolymer of glycolic acid and lactic acid (col 9, lines 60-64) as alternatives as in claim 60. The decellularized tissues suggested by Goldstein, Bishopric et al and Livesey et al are devitalized as required by claim 71.

Oppermann et al suggest an osteogenic protein as in claim 73 having a 6- or 7-cysteine skeleton (paragraph bridging cols 5 and 6).

Double Patenting

Claims 49-53, 55-60 and 70-106 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-30 of U.S. Patent No. 6,110,482 or claims 1-9 of U.S. Patent No. 5,906,827 or claims 1-19 of U.S. Patent No. 6,027,743. Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed device and method of use requiring an osteogenic protein and matrix would have been obvious from the same type of device and/or method of use requiring an osteogenic protein and matrix as claimed by the claims of the patents.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David M. Naff
Primary Examiner
Art Unit 1651

DMN
5/25/04